UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,370	05/17/2002	Charles Andrew Collyer	229752001500	1330

25226 7590 03/21/2005

MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

EXAMINER	
MONDESI, ROBERT B	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 03/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,370	COLLYER ET AL.	
	Examiner	Art Unit	
	Robert B Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *12-17 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,18 and 19* is/are rejected.

7)☒ Claim(s) *9 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 May 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 07, 2004 has been entered.

Status of the Claims

Presently **claims 1-20** are pending. **Claims 12-17 and 20** are withdrawn for pertaining to non-elected subject matter. **Claims 1-11 and 18-19** are currently under examination.

Withdrawal of Objections and Rejections

The rejection of **claims 1-10, 18 and 19** under 35 U.S.C § 103(a) as being unpatentable over Patempa et al. in view of Nakayama et al. (cited in IDS, paper #6) and Bramanti et al. is withdrawn

The rejection of **claim 11** under 35 U.S.C. 103(a) as being unpatentable over Progulske-Fox et al. in view of Nakayama et al. (cited in IDS, paper #6) and Bramanti et al. is withdrawn

New Rejection(s) and objection(s)

Claim Objections

Claims 9 and 11are objected to for not complying with the requirements of 37 CFR 1.821. The claims contain sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, the fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below: Nucleic acid sequences longer than 10 nucleotides and amino acid sequences longer than 4 resides need to be designated with a sequence identifier. Applicants must correct the sequence submissions in the mentioned claims. Examiner would like to point out that <400>6 in claim 9, line 11; <400>1, lines 5 and 7; <400>8, in lines 6 and 7, and <400>7 in line 8 are not proper sequence identifications of referenced sequences. These sequences need to be referred to with specific SEQ ID No:s that are present in the written sequence listing submission such as SEQ ID No: 6, 1, 8 and 7.

Specification

The disclosure is objected to because of the following informalities: This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below: Nucleic acid sequences longer than 10 nucleotides and amino acid sequences longer than 4 resides need to be designated

with a sequence identifier. Applicants must correct the sequence submissions in the specification on e.g.: Page 8, lines 14-15; page 10, lines 1-10; page 17, lines 5-32; page 10, lines 12 and 14; page 21, lines 11 and 13; page 24, lines 1-2, 4, 10, 17-18 and 20; page 37, lines 28-29; page 40, lines 27-29; page 44, line 8. As mentioned above these sequences need to be referred to by a proper sequence identifier such as a SEQ ID No:.

Also the Brief description of drawings does not match identifiers, e.g. "2" instead of "2a-2b"; "3" instead of "3a-3b" and etc.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 and 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of an infection by a microorganism, does not reasonably provide enablement for prophylaxis of an infection by a microorganism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a

correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1.Breadth of the claims.

In regards to the method of the invention and the breadth of the claims the broadest interpretation that applies is a method for prophylaxis or treatment of an infection by a microorganism comprising administering an effective amount of an agent that will antagonize the interaction between a molecule having an HA2 domain and an HA-2 binding motif on a porphyrin containing molecule.

2. The nature of the invention.

The nature of the invention is a method for prophylaxis or treatment of an infection by a microorganism comprising administering an effective amount of an agent that will antagonize the interaction between a molecule having an HA2 domain and an HA-2 binding motif on a porphyrin containing molecule.

3. The state of prior art.

The state of the prior art does not provide any methods with regards to prophylaxis of infections comprising administering an effective amount of an agent that will antagonize the interaction between a molecule having an HA2 domain and an HA-2 binding motif on a porphyrin containing molecule. However, the prior art does provide supporting evidence for the treatment of infections caused by microorganisms via the use of the method of the invention. Nakayama et al. have isolated a hemoglobin-binding protein associated with the outer membrane of *P.gingivalis* and identified this protein as one homologous with the HA2 domain of gingipains. Nakayama et al. reported that, adsorption of hemaeglobin to whole *P.gingivalis* cells was associated with the presence of the HA2 domain and furthermore, hemin accumulation within the *P.gingivalis* cells was shown to be dependent on functional expression of KGP; hence the HA2 gingipain domain has been predicated to function as a hemoglobin-binding domain. It should be noted that the prior art also states that the passive uptake through the outer membrane of gram-negative bacteria is not a significant route of heme entry and most bacteria posses specific heme uptake systems to use this compound either as iron or iron-porphyrin source. In most gram-negative bacteria heme utilization is mediated by specific outer membrane receptors that bind directly to host heme-sequestering protein. *P.gingivalis*, the etiological agent of adult periodontal disease, has been shown to require hemin for growth (Genco et al.).

4. The relative skill in the art.

The relative skill in the art as it relates to the administering of therapeutic polypeptides used for the treatment, inhibition, prevention or amelioration of pancreatic disorder is characterized by that of a M.D. or Ph. D. level individual.

5. The level of predictability in the art.

The level of predictability in the art in view of prophylaxis is extremely low since that are no viable animal models demonstrating the effectiveness of the method of the invention with regards to prophylaxis. However the prior art does present some in vitro data that is indicative of a method of treatment of an infection by a microorganism comprising administering an effective amount of an agent that will antagonize the interaction between a molecule having an HA2 domain and an HA-2 binding motif on a porphyrin containing molecule. Progulske-Fox disclose; DNA fragments from *P.gingivalis* which express hemagglutinin (HA) proteases that elicit anti- *P.gingivalis* responses, microorganisms genetically modified to express *P.gingivalis* antigens and antibodies for the detection and treatment of periodontal disease. Progulske-Fox disclose multitudes of in vitro assays demonstrating the effectiveness of the compositions of he invention with regards to the treatment of periodontal disease.

6. The amount of guidance present.

Due to lack of any viable working animal models in the applicants' disclosure and the lack of the same in the prior art with the regards to prophylaxis, the amount of guidance present is extremely low. However given the nature and extent of in vitro studies there is sufficient amount of guidance for a method of treatment of an infection by a microorganism comprising administering an effective amount of an agent that will

antagonize the interaction between a molecule having an HA2 domain and an HA-2 binding motif on a porphyrin containing molecule.

7. The existence of working examples.

Applicants have provided experimentation structured towards an in vitro climate as exhibited on pages 37-51 of the specification. In order for an experiment to provide data that is indicative of prophylaxis, the experiment must be performed in an in vivo environment involving the subject animal that is to be targeted for a method of prophylaxis. Consequently, the experimentation provided by the applicant can only be considered as evidence in support of a method of treatment.

8. The quantity of experimentation necessary.

In the case of prophylaxis more experimentation would be required to practice the invention since the specification has not shown to a person skill in the art how to use the invention.

Due to the large quantity of experimentation necessary to provide evidence that the claimed method of the invention will lead to prophylaxis of infection caused by a microorganism, the lack of guidance presented in the specification regarding the same, the absence of a working example directed to same, the unpredictable nature of the invention with regards to prophylaxis, the state of the prior art not providing any evidence for any method for prophylaxis of an infection by a microorganism comprising administering an effective amount of an agent that will antagonize the interaction between a molecule having an HA2 domain and an HA-2 binding motif on a porphyrin containing molecule., and the breath of the claims which fails to provide particular steps

involved in the prophylaxis of an infection caused by a microorganism, the specification fails to teach the skilled artisan in the art how to make and use the invention.

With regard to **claim 9**, directed to a polynucleotide sequence that hybridizes to the disclosed sequences, Applicants have not sufficiently defined the conditions under which the hybridizations are to take place. Nucleic acid hybridization assays are extremely sensitive to the conditions in which they are performed. The buffer composition, pH, temperature, length of time, salt concentrations, quality and source of template nucleic acid, are all variables which determine the reproducibility of a given hybridization experiment. Given the unpredictability of the art and the nature of hybridization experiments in general, it is not sufficient to merely cite hybridization without a clear and explicit recitation of the conditions associated with the hybridization. For example, the definition of stringency as it pertains to hybridization conditions is subject to interpretation and is different from laboratory to laboratory. Therefore, without a clear and explicit recitation of the conditions in the claim, which were actually used by Applicants in isolating the claimed polynucleotides, which hybridize to the disclosed sequences, the skilled artisan would not be able to practice the claimed invention and would not be reasonably apprised of the metes and bounds of the claimed invention. Without such guidance, the experimentation left to those skilled in the art is undue. Including in the claims the exact nature of the hybridization conditions used to isolate the claimed polynucleotide would aid in overcoming this portion of the rejection.

Claims 1-11, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In **claims 1-11, 18 and 19** the applicants cite the presence of a HA-2 domain. It is noted that this is merely a generic identification of a peptide that is specifically defined. The abbreviation HA-2 stands for a particular domain of the polypeptide Hemagglutinin that consists of a specific amino acid sequence. The applicants need to define the specific sequence of the cited peptide in the form of a SEQ ID No: in order to overcome the ambiguities that arise when a generic abbreviation is used to define a specific peptide.

In **claim 1** the applicants state that the method of the invention comprises administering an effective amount of an agent for a time and under sufficient conditions; however the applicants have not explained the amount of time, as in minutes or hours, that is considered to be "for a time", neither have the applicants explained the extent of "sufficient" with regards to conditions for antagonizing the interaction between a molecule derived from a microorganism having an HA2 domain and an HA2-binding motif on a prohyrin containing molecule.

In **claim 2** the applicant cites the phrase "related organism" but fails to explain in the specification of the present application the nature of these related organisms.

Regarding **claims 6, 8-9, 11** the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 9-11, 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Potempa et al. in view of Progulske-Fox and Nakayama et al.

Potempa et al. teach that their invention provides for methods of protecting a mammal, including human, from periodontitis and or other pathology caused at least by *P. gingivalis* said method comprising the step of administering to said mammal an immunogenic composition comprising at least one hemaglutinin peptide component wherein the peptide confers protection against infection caused by *P. gingivalis* when administered to a patient (page 3, lines 20-35 and page 4 lines 10-13).

Potempa et al. do not teach that the interaction between a hemaglutinin peptide and a hemaglutinin motif on a porphyrin molecule is antagonized.

Progulske-Fox teaches a method of detecting the presence of disease causing *P. gingivalis* and discloses polypeptides, which can be used for the production of antibodies to the organisms associated with periodontal disease and in view of the immunoprotectant activity exhibited by certain compositions of matter of the subject invention, vaccines may be produced from the polypeptides expressed by cells which have been transformed with DNA fragments from *P. gingivalis*. By introducing these peptides, along with pharmacologically suitable vehicle, into the human or animal host, that host can be induced to generate immunological protection against *P. gingivalis* (page 41, 24-29).

Progulske-Fox also teaches that the *P. gingivalis* hemagglutinin protein was expressed in non-virulent *Salmonella typhimurium* strain SL326/CL7 and tested for activity as a competitive inhibitor of hemagglutination.

Progluski et al. do not teach that the hemagglutinin molecule is HA-2.

Nakyama et al. teach that the hemagglutinnn molecule is HA-2 (page 52 lines 12-24.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine Potempa et al. Progulske-Fox and Nakyama et al. for the advantages of a method of treatment of periodontal disease comprising administering an effective amount of an agent that will antagonize the interaction between a molecule having an HA2 domain and an HA-2 binding motif on a porphyrin

containing molecule. Because the antagonizing effect of the mentioned agent leads to the inhibition of the hemagglutinating activity of *P. gingivalis* , which has been shown to play an important role in the survival of the *P. gingivalis* in the periodontal pocket, and will reduce colonization of *P. gingivalis* in areas of infection as taught by Potempa et al., page 3, lines 20-25 and Progulske-Fox et al., page 2 lines 9-14.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert B. Mondesi

JON WEBER
SUPERVISORY PATENT EXAMINER